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Cystosarcoma Phyllodes of the Breast

A Statistical Study of Forty Cases

by

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1. INTRODUCTION

Cystosarcoma phyllodes is described in the textbook as a subclass of Fibroadenoma. Fibroadenoma is microscopically made up of two components, a proliferating connective tissue stroma and an atypical multiplication of duct and acini. Cystosarcoma phyllodes which was described first by JOHANNES MUELLER meant originally benign. It seems that it was named by clinical and pathological features. Frequency of this tumor is lower than Fibroadenoma.

We have experienced 40 cases of Cystosarcoma phyllodes and 361 cases of Fibroadenoma during the ten year period from 1958 to 1967 in the Second Surgical Clinic, Kyoto University Hospital. Cystosarcoma phyllodes therefore is about 10% of Fibroadenoma. We compared these two types statistically.

The adjustment of these statistics came about, when a woman would have two or more tumors in her breast, the largest one being represented, and when a similar tumor grew on the opposite side afterwards, the former one was represented.

2. STATISTICAL RESULTS

A) Frequency

A total of patients with breast diseases who have consulted our clinic during the ten year period from 1958 to 1967 was shown in Table 1. Cystosarcoma phyllodes was 1.4%, and Fibroadenoma was 12.7%. Forty cases of Cystosarcoma phyllodes was shown in Table 2.

Frequency of Cystosarcoma phyllodes in our clinic was lower than HAAGENSEN's report. HAAGENSEN reported that frequency of Cystosarcoma phyllodes was 2% of Fibroadenoma.

B) Age

In our series of cases, the youngest patient with Cystosarcoma phyllodes was 13 and the oldest 49, the youngest with Fibro-

Table 1 A total of the patients with breast diseases (1958-1967)
Second Surg., Kyoto Univ. Hospital

Breast diseases	Number of cases	Percentage
Mastopathia	1123	39.6%
Breast Cancer	576	20.3
Fibroadenoma	361	12.7
Inflammation	178	6.3
Gynaecomastia	138	4.9
Mazoplasia	115	4.1
Mastodynia	101	3.6
Cystosarcoma phyllodes	40	1.4
Ductectasia	29	1.0
Foreign body inflammation	7	0.2
the others	169	5.9
Total	2837	100.0%

Table 2 The clinical and pathologic findings in the forty patients with Cystosarcoma phyllodes

Case No.	Age (yrs.)	Marriage	Duration from discovery to consultation	Diameter	Location of the tumor	Times of the pregnancy	Times of the delivery	Histological finding	Treatment	Follow-up
1	25	S	y. 6m.	4× 3cm	L : up, i	0	0	benign	simple excision	9y. 1m. well
2	46	M	2	6× 6	R : w	1	1	borderline	radical mastectomy	8 7 well
3	27	S	1 5	7× 3	L : up, i	0	0	benign	simple excision	none
4	15	S	5	6× 5	L : up, i	0	0	benign	simple excision	8 3 well
5	34	M	1	7× 5	L : up, l	2	1	benign	simple mastectomy	7 well
6	45	M	9	10×10	R : w	3	3	borderline	radical mastectomy	7 7 well
7	31	M	2 2	5× 4	L : un. l	2	1	benign	simple excision	6 8 well
8	16	S	2	17×16	R : w	0	0	borderline	simple excision	6 8 well
9	38	M	1 8	17×15	R : w	1	1	borderline	radical mastectomy	5 11 well
10	26	S	6	5× 4	L : up, l	0	0	borderline	simple excision	none
11	18	S	1 1	6× 5	R : un. l	0	0	borderline	simple excision	4 9 well
12	20	S	4	5× 4	L : up, i	0	0	benign	simple excision	3 5 well
13	36	M	5	6× 6	L : up, i	0	0	benign	simple excision	4 2 well
14	13	S	2	8× 8	L : up, l	0	0	benign	simple excision	5 well
15	45	M	2d.	4× 3	L : un. l	6	3	benign	simple excision	2 6 well
16	49	M	6	12×10	R : w	1	1	benign	simple mastectomy	4 5 well
17	26	S	2	5× 3	L : up, l	0	0	benign	simple excision	none
18	14	S	3	7× 6	R : un. l	0	0	benign	simple excision	4 1 well
19	23	M	3	12×12	R : w	0	0	benign	simple excision	3 10 well
20	17	S	2	10× 8	R : un. l	0	0	benign	simple excision	3 7 well
21	18	S	3	9× 6	L : up, l	0	0	benign	simple excision	2 7 well
22	45	M	2	15×15	L : w	1	0	benign	simple mastectomy & axillary dissection	3 well
23	41	M	9	15×15	L : w	0	0	borderline	simple mastectomy & axillary dissection	2 10 well
24	18	S	3	8× 8	R : up, l	0	0	borderline	simple excision	2 8 well
25	26	S	5	5× 4	R : up, i	0	0	benign	simple excision	2 7 well
26	21	S	3	9× 9	L : up, i	0	0	benign	simple excision	2 6 well
27	26	M	5	7× 7	L : up, i	1	1	benign	simple excision	none
28	23	S	2	4× 3	L : up, i	0	0	benign	simple excision	2 6 well
29	27	S	2	3.1×2.4	R : un. l	0	0	benign	simple excision	1 1 well
30	20	S	3	5× 5	L : up, i	0	0	benign	simple excision	1 11 well
31	23	M	2	3× 2	R : up, i	2	1	—	no excision	increased
32	18	S	3	3×2.5	L : up, i	0	0	benign	simple excision	9 well
33	19	S	3d.	2.5×2.5	L : up, i	0	0	benign	simple excision	1 4 well
34	18	S	3	3.4×3.4	R : up, i	0	0	benign	simple excision	2 well
35	28	M	7	4× 3	R : un. l	1	1	benign	simple excision	11 well
36	23	S	1	12×12	R : w	0	0	benign	simple excision	9 well
37	21	S	1 10	4.5×4	L : un. l	0	0	benign	simple excision	8 well
38	23	S	3	3× 3	R : up, i	0	0	benign	simple excision	7 well
39	18	S	5	2.5×2	L : up, l	0	0	benign	simple excision	6 well
40	21	S	4	3.5×3.5	R : up, i	0	0	benign	simple excision	2 well

S : single female M : married female up : upper un : under i : inner l : lateral
w : whole breast

adenoma 13 and oldest 56. The greatest number of Cystosarcoma phyllodes and Fibroadenoma occured in patients in the second decade, but the second largest frequency occured between the ages 10-19 in Cystosarcoma phyllodes and between the ages 30-39 in Fibroadenoma (Fig. 1, Table 3). Furthermore each of these percentage is much alike. The percentage distribution of ages with our cases of Fibroadenoma had almost the same tendency as HAAGENSEN's but Cystosarcoma phyllodes was different. HAAGENSEN stated that Cystosarcoma phyllodes occurs at a later age than ordinary Fibroadenoma and the average age of the patients with Cystosarcoma phyllodes was 45.1 years. The average age in our series of cases was 26.0 years (Table 4). On the contrary, the average age in our series of cases with Fibroadenoma was almost the same as HAAGENSEN's, that is; HAAGENSEN's 33.5, ours 29.0. In our series of cases, the percentage of the patients with Fibroadenoma who were more than forty years old was 12.8% and Cystosarcoma phyllodes 15.0%. But many authors in Japan report

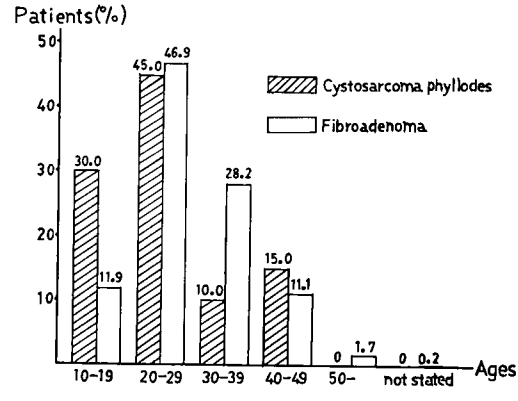

Fig. 1 Percentage distribution of ages in 40 patients with Cystosarcoma phyllodes and in 361 with Fibroadenoma.

Table 3 Ages

	Cystosarcoma phyllodes		Fibroadenoma	
Ages	Number of the patients	Percentage	Number of the patients	Percentage
10—19	12	30.0%	43	11.9%
20—29	18	45.0	169	46.9
30—39	4	10.0	102	28.2
40—49	6	15.0	40	11.1
50—	0	0.0	6	1.7
not stated	0	0.0	1	0.2
Total	40	100.0%	361	100.0%
Average age	26.0 yrs.		29.0 yrs.	

Table 4 Average age

Authors	Year	Cystosarcoma phyllodes		Fibroadenoma	
Treves	(1951)	40.9 yrs.	(77 cases)		
Stout	(1954)	44	(55)		
Haagensen	(1956)	45.1	(36)	33.5 yrs.	(510 cases)
Hafner	(1962)	46	(12)		
Amaaki	(1964)	23.5	(15)		
Harold	(1965)	49	(18)		
Second Surg. Kyoto Univ. Hospital	(1968)	26.0	(40)	29.0	(361)

that Cystosarcoma phyllodes were with young woman, also AMAAKI stated that the average age of the patients with Cystosarcoma phyllodes was 23.5 years. Thus Cystosarcoma phyllodes in our country appears in young women. It is not clear that this means the difference of a race. In our series of cases only one patient with Cystosarcoma phyllodes was in the menopause and others were in the time from puberty to menopause. In regard to the youngest age, REIHER reported a 12 years girl who had Cystosarcoma phyllodes on both of her breasts. SHIROTA reported a 11 years old girl who had been in the premenstrual time. IWASA also reported a 11 year old girl whose tumor had 555 g weight. These two cases are thought to be the youngest cases in history. In our series of cases the youngest one was 13. Therefore, apart from predirection age Cystosarcoma phyllodes develops at a young age as well as middle age.

C) Marriage

It is said that Cystosarcoma phyllodes is frequent in unmarried woman, but in our series of cases as shown in Table 5, the unmarried women were 65.0% and Fibroadenoma 43.5%. It seems to us that age factor is the cause of this result.

Table 5 Marriage

	Cystosarcoma phyllodes	Fibroadenoma
single female	26 cases (65.0%)	157 cases (43.5%)
married female	14 (35.0)	204 (56.5)
Total	40 cases(100.0%)	361cases(100.0%)

D) Duration from discovery to consultation

This discovery means the consciousness of symptoms. As shown in Table 6, many cases of Cystosarcoma phyllodes were left alone for more than five years. The percentage of the patients with Cystosarcoma phyllodes who consulted our clinic within one year was 50.0% and a large majority of cases with Fibroadenoma was 75.3%. It seems that some long existing Fibroadenoma develops into Cystosarcoma phyllodes at a certain time and grows rapidly.

Table 6 Duration from discovery to consultation

	Cystosarcoma phyllodes		Fibroadenoma	
Duration	Cases	Percentage	Cases	Percentage
within 2 weeks	2		72	
1 month	0	20 50.0%	57	272 75.3%
6 months	14		92	
1 year	4		51	
5 years	17	20 50.0	74	86 23.9
longer than 5 years	3		12	
not stated	0		3	0.8
Total	40	100.0%	361	100.0%

E) Size of tumor

The size was expressed by the longest diameter.

About half of the patients with Cystosarcoma phyllodes were within 3-5 cm in diameter, about half of Fibroadenoma were less than 1 cm, two cases of Fibroadenoma were 6 cm, and five cases of Cystosarcoma phyllodes were less than 3 cm (Table 7). HAAGENSEN reported that the size of Cysto-

Table 7 Size of the tumor

Diameter	Cystosarcoma phyllodes	Fibroadenoma
smaller than 1 cm	0 cases	180 case
2	0	94
3	5	45
4	7	22
5	7	5
6	4	2
7	4	0
8	2	0
9	2	0
larger than 10	9	0
not stated	0	13
Total	40 cases	361 cases

arcoma phyllodes was within 4-28 cm in diameter and most of them were within 4-9 cm. In our series of cases, the largest one was 17 × 16 cm in diameter.

F) Location

The location of Cystosarcoma phyllodes and Fibroadenoma were almost similar with the breast cancer but it was peculiar that 27.5% of the patients with Cystosarcoma phyllodes had it situated in left upper inner quadrant (Fig. 2, 3). Moreover, 22.5% of the patients with Cystosarcoma phyllodes had it occupy the whole breast.

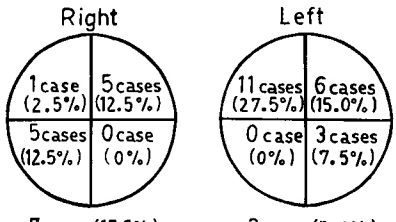

Fig. 2 Anatomical location of Cystosarcoma phyllodes.

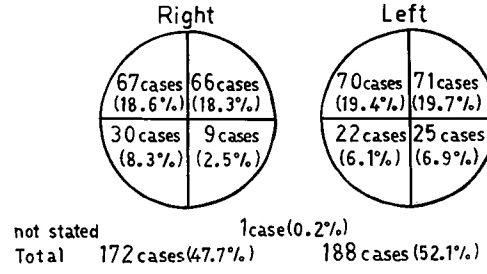

Fig. 3 Anatomical location of Fibroadenoma.

3. CONSIDERATION

As stated above, we compared Cystosarcoma phyllodes with Fibroadenoma which we experienced during ten years in our clinic but their classification is fairly difficult. Both of them are fibroadenomatous tumors which occur in the breast. That is, there are the increase of stromal and epithelial component in both types.

STOUT had applied the term Cystosarcoma phyllodes to the circumscribed usually bulky fibroepithelial tumors with unusually cellular stroma suggestive of sarcoma and exclusively rapid growing tumor even if there is no cellular stroma suggestive of sarcoma.

Concerning the fibroepithelial tumor which included in Fibroadenoma, when the epithelial component is numerous, it is said adenoma, and when fibrous component is numerous, it is said fibroma though pure fibroma is rare. When there is myxoid degeneration of stroma it is said myxoma, and when this myxoid change is accompanied by cystic change the lesion is said to be Cystosarcoma phyllodes. Moreover, when there is proliferation toward duct, it is called intracanalicular fibroadenoma, when there is proliferation around duct, it is called pericanalicular fibroadenoma. But there are originally no difference, and frequently both types appear in the same tumor.

A) Concept of Cystosarcoma phyllodes

Cystosarcoma phyllodes was described by JOHANNES MUELLER, in 1838. Depending upon the pathological concept, sarcoma is originally the malignant tumor. It is generally known that MUELLER did not mean sarcoma for a malignant tumor but he named it means of mass. Some one says that the word "sarcoma" gives an impression of malignancy so it is not proper. Other workers give many synonyms according to the partial feature of this tumor as shown in Table 8. But none of these synonyms include whole histological and clinical features of this tumor. Cystosarcoma phyllodes is considered a subclass of Fibroadenoma but there are many definitions. NORMAN TREVES stated that the great

Table 8 Synonyms of Cystosarcoma phyllodes

1) Adenocystosarcoma
2) Adenoma pseudosarcomatodes
3) Adenomyxoma (Wilms)
4) Adenosarcoma
5) Alveolar sarcoma
6) Angioectatic sarcoma
7) Brodies serocystic disease of breast
8) Brodies tumor
9) Cystosarcoma phyllodes
10) Carcinosarcoma
11) Cellular hydatids (Cooper)
12) Composite cystoids
13) Cystoadenoma phyllodes
14) Cystoadenosarcoma
15) Cystofibroma papillare
16) Cystoma papilliferum
17) Cystosarcoma
18) Cystosarcoma arborescens
19) Cystosarcoma intracanaliculare
20) Cystosarcoma papillare
21) Cystosarcoma poliposum intracanaliculare
22) Cystosarcoma proliferum
23) Fibroadenoma intracanaliculare fibromatosum
24) Fibroadenoma intracanaliculare sarcomatodes xantomatodes
25) Fibroadenoma phyllodes (benign, malignant)
26) Fibrocystoadenoma intracanaliculare
27) Fibromyxoma intracanaliculare obliterans
28) Fibrosarcoma
29) Gelatinous cystosarcoma
30) Giant fibroadenoma
31) Giant intracanaliculare fibroadenomyxoma
32) Giant intracanaliculare myxoma of the breast
33) Giant mammary myxoma
34) Glandular proliferous cysts
35) Indigenous sarcoma
36) Intracanalicular myxoma (Virchow)
37) Intracanalicular sarcoma
38) Malignant fibroadenoma
39) Miniature cystosarcoma phyllodes
40) Mixed tumor of the breast
41) Mutation tumor
42) Pearly cystosarcoma phyllodes
43) Periductal sarcoma
44) Pseudosarcoma
45) Serocystic sarcoma
46) Simple cystosarcoma
47) Tuberous cystic tumor of the breast
48) Proliferous cystosarcoma

increase of the stromal part was included in Cystosarcoma phyllodes and greatness was a secondary problem, this is by increase of quantity and of cellular part or both. Thus he excluded the tumor which simply microscopically Fibroadenoma even though large, and included the tumor which had increasing stroma even though small. HAAGENSEN included Fibroadnoma that had large size or rapid growing tumor, in Cystosarcoma phyllodes. STOUT applied the term Cystosarcoma phyllodes to the circumscribed usually bulky fibroepithelial tumors with unusually cellular stroma suggestive of sarcoma and exclusively rapid growing tumor even if there was no cellular stroma suggestive of sarcoma as stated above.

Generally, it is not large and can be determined it by its histological picture and clinical course. On the ground that Cystosarcoma phyllodes and Fibroadenoma are originally the same, we included it in Cystosarcoma phyllodes which had a giant size, great increase invelopment, and its stroma has follicular, great density of cellurality.

B) Clinical symptoms

Usually the patient becomes aware of her tumor without pain. This is the same in Cystosarcoma phyllodes and Fibroadenoma, but duration from discovery to consultation is longer in the former. Nipple retraction, ulceration of the skin, nipple discharge or adhesion with the surrounding tissues are very few. In our series of cases, only two cases complained of pain and all other cases were painless. Ten cases had the venous dilatation upon the overlying skin (Fig. 4). Five cases had Fibroadenoma in the other side.

C) Pathological features

Macroscopical; The cut surface shows the foliated structure, in some place, cyst of

various size, bleeding, myxoid degeneration or colloidal change are visible. At times a cartilagenous change is visible. Fig. 5 is the cut surface of Case 36. In this tumor, cysts are not visible but foliated structures are visible. It seems the gathering of tumors that are divided by connective tissues. Fig. 6 is the cut surface of Case 23, bleeding within the cyst, collagenous change are visible. It seems that the tumor surrounded entirely by the thick capsule.

Microscopical; Characteristic pictures of Cystosarcoma phyllodes are that proliferation of stroma is much greater than Fibroadenoma (Fig. 7) and riches in cellural component (Fig. 8, 9), so it looks liks as a pattern of differenciated sarcoma. Besides, foliated protrusions of stroma are marked alike in intracanalicular type of Fibroadenoma. Edema, myxoid degeneration, cartilageous change are rarely seen. As stated above, histological pictures of Cystosarcoma phyllodes are variable by plane. Fig. 10, 11 are histological pictures of Case 2, anaplasia of stromal cells, increase of stromal component are seen. But the clinical course was well, so this case is thought to be the "borderline group" as described by TREVES. Giant cells are not seen in this case.

D) Clinical course

MUELLER and many other authors emphasize that Cystosarcoma phyllodes is the benign tumor. But it is rarely malignant and metastasize haematogenously to the lung, bone, liver,

Fig. 4 Case 36 23 yrs. Pigmentation, venous dilatation are seen.

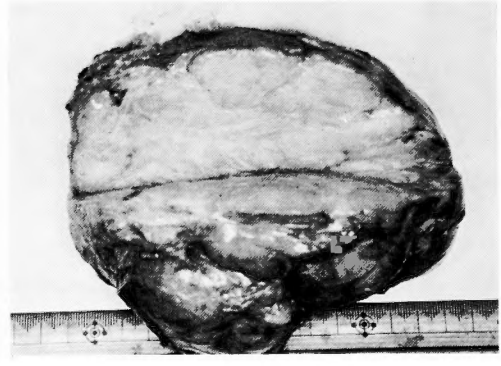

Fig. 5 The cut surface of the Case 36

Fig. 6 The cut surface of the Case 23. Bleeding within the cyst, collagenous change are seen.

Fig. 7 A histological picture of the Case 23. The foliated protrusion of the stroma is marked (H. & E., ×40)

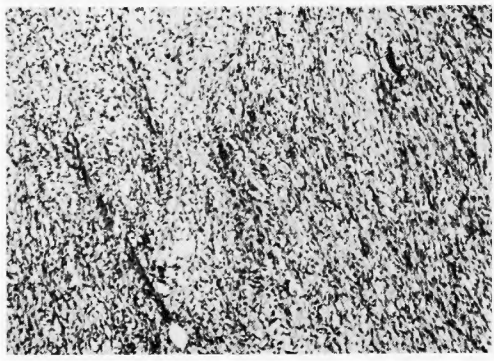

Fig. 8 A histological picture of the Case 23. This is riched in cellural component and it looks like as a pattern of the differenciated sarcoma. (H. & E., ×40)

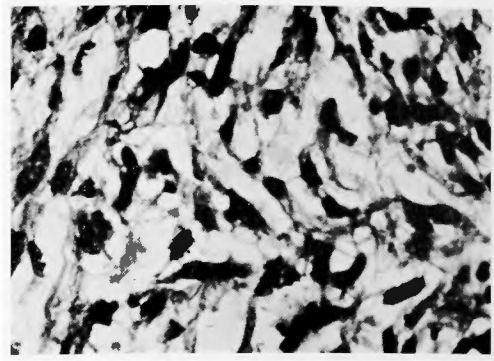

Fig. 9 Magnified picture of the Case 9. (H. & E., ×400)

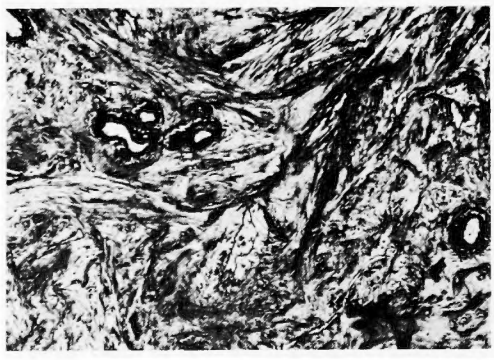

Fig. 10 Case 2 (H. & E., ×100)

Fig. 11 Case 2 (H. & E., ×200)

etc. We can see few reports of metastasis to the lymph node. Some part of Cystosarcoma phyllodes include the stromal part which imply very little malignancy, but its clinical course is quite benign in most cases. In our series of cases, there were seven cases which had anaplasia of stromal cells and mitosis but these clinical courses were well. We followed up 36 cases, as shown in Table 2, there were no recurrences except in Case 29. As to Case 31 who refused the operation, the tumor was continued to grow.

TREVES stated that the earliest indication of malignant change of a tumor in his series had been marked focal cellularity and anaplasia of the stroma situated near the epithelial structures, moreover, the occurrence of bizarre giant cells in an otherwise benign appearing stroma was not at present considered to be an indication of potential clinically malignant behavior. LESTER and STOUT agree with him for the most part but there were a few metastsing cases without these pictures. So they warn that it is dangerous to decide the prognosis and the method of treatment only with the histological pictures. The malignant appearing area in the truly malignant Cystosarcoma phyllodes may be so small that only meticulous study of many sections from the entire tumor will find it. Therefore one should decide the methods of treatment by histological pictures from multiple sections and clinical features.

E) Treatment

As most of Cystosarcoma phyllodes is benign, it will suffice to remove the tumor including a few normal parts of the surrounding breast tissue. The surgical procedure performed in our series are shown in Table 9. The radical mastectomy was performed in three cases because they were diagnosed malignant by clinical features and pathological pictures with frozen sections at the time of operation.

Table 9 Type of the operation

Type	Cases
Simple excision	32
Simple mastectomy	2
Simple mastectomy & Axillary dissection	2
Radical mastectomy	3
Total	39

F) Results of treatment

In our series of cases, as Case 8, four years later Fibroadenoma were found in her right breast 4 cm apart from previously excised part and in her left breast. As with Case 24, three years ago Fibroadenoma in her left breast was excised, then Fibroadenoma developed again apart from 3 cm from previous wound but the tumor was found in her right breast as well. This tumor in her right breast developed to Cystosarcoma phyllodes. As with Case 29, she had performed partial excisions of bilateral Cystosarcoma phyllodes and eight months later bilateral tumors was found again, but now we observe her because she refused the excision, however, these tumors are increasing in their size.

4. SUMMARY

40 cases of Cystosarcoma phyllodes were compared with 361 cases of Fibroadenoma statistically.

1. It is of interest to note that Cystosarcoma phyllodes is frequent in young women in our country.

2. We think that there is originally no difference histologically between Cystosarcoma phyllodes and Fibroadenoma.

3. Most Cystosarcoma phyllodes are benign, so one can get through by a little operative invasion in majority of cases.

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和文抄録

乳腺葉状嚢肉腫

40例の統計的観察

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最近10年間に我々の経験した葉状嚢肉腫40例を線維腺腫361例と統計的に比較検討し，文献的考察を加えた．その結果，次の3点を認めた．

1. 我が国では葉状嚢肉腫は若い女性に多い．
2. 葉状嚢肉腫と線維腺腫とは本質的に差異はない．
3. 葉状嚢肉腫の大部分は良性なので，手術侵襲は小さくてすむことが多い．